

Amendments to the Specification

Please replace the paragraph spanning pages 4 and 5 with the following:

- Figures 2A-2B represent the sequence alignments. (aA): alignment of the P domains of TWIK-1 (SEQ ID NOS:9 and 10), TOC/YORK and other representative K⁺ channel families (SEQ ID NO:11 through SEQ ID NO:23); the identical and conserved residues are circled in black and in gray, respectively. (b): alignment of TWIK-1 (SEQ ID NO:2) with potential homologs of; the sequences M110.2 (SEQ ID NO:7) and F17C8.5 (SEQ ID NO:6) were deduced from the gene sequences (respective access numbers Z49968 and Z35719); the computerized splicing of the other genomic sequences of *C. elegans* (respective access numbers Z49889, P34411 and Z22180) is not sufficiently precise to allow their perfect alignment and is therefore not shown.

On page 5, please replace the last paragraph with the following:

- Figure 5 shows the properties of the single TWIK-1 channel (SEQ ID NO:2). (a): current tracings recording in the input-output configuration to the membrane potentials indicated in the absence (m) or in the presence (.) of internal M²⁺ (3 mM) and in symmetry with 140 mM of K⁺. (b): mean of curves I-V (n = 10). (c and d): open time of distribution obtained at +80 mV (top histograms) and at -80mV (bottom histograms) in the presence of 3 mM Mg²⁺ (c) or in the absence of Mg²⁺ (d).

On page 6, please replace the first paragraph with the following.

- Figure 6 shows the blocking of the TWIK-1 channels (SEQ ID NO:2) by the internal pH. (a and b): blocking effect of the internal acidification on the TWIK-1 currents, induced by perfusion of CO₂; (a) tracings of superimposed currents induced by a depolarization phase at -30mV starting at HP = -80 mV, control (top tracing), effect when equilibrium is reached in the presence of CO₂ (bottom tracing); (b) graph (n = 5) showing the almost complete blockade of the TWIK-1 currents induced by CO₂; (c and d): internal acidification induced by the application of DNP (1mM). (c): same protocol as in (a), control (top tracing) and after 5 minutes of application of DNP (bottom tracing); (d): graph (n = 4) indicating the percentage of TWIK-1 current remaining after treatment with DNP. (e and f): imposed voltage (method: attached patch) under symmetrical conditions of K⁺ concentration (140 mM) maintained at +80mV. (e) course over time of the effect of 1 mM of DNP (marked with arrow) on the activities of the single TWIK-1 channel. (f): graph (n = 4) showing the effect of DNP on the mean probability of opening NP_o calculated during 1 minute of recording starting at the equilibrium state. (g): activities measured in the “inside-out patch” state at 80 mV at different internal pH values. Bar graph (n = 10) of NP_o in relation to the internal pH.

On page 6, please replace the last paragraph with the following:

- Figure 7 shows the activation of the TWIK-1 channels (SEQ ID NO:2) by PMA, activator of protein kinase C. (a): perfusion of PMA (30nM) for 10 minute increases the TWIK-1 current (top tracing) induced by a depolarization phase at +30 mV starting at HP = 80 mV, control current (top tracing). (b): graph (n = 5) showing the activation effect of PMA on the TWIK-1 currents. (c and d): attached patch configuration under symmetrical K⁺ concentration

conditions maintained at +60 mV; (c): course over time of the effect of 30 nM of PMA on the single channel activities; the recordings of the channel activity were performed with a rapid scanning before and after the application of PMA; (d): bar graph (n = 5) showing the activation effect of PMA on NP_o.

On page 7, please replace the first paragraph with the following:

- Figure 8A-8B show the nucleotide and deduced amino acid sequences of human TASK (SEQ ID NO:3) and partial amino acid sequence of mouse TASK (SEQ ID NO:5). Consensus sites for N-linked glycosylation (*) and phosphorylation by protein kinase C (n), protein kinase A (s) and tyrosine kinases (1) in human TASK (SEQ ID NO:4). These sites have been identified by using the prosite server (European Bioinformatics Institute) with the ppsearch software (EMBL Data library) based on the MacPattern program. The sequence of human and mouse TASK have been deposited in the GenBank/EMBL database under the accession numbers AF006823 and AF006824, respectively.

On page 7, please replace the third paragraph with the following:

- Figure 10 shows the ~~northern~~Northern blot analysis of TASK (SEQ ID NO:4) distribution in adult human tissues. Human multiple tissues Northern blots from Clontech were probed at high stringency with a TASK cDNA probe. Each lane contains 2 µg of poly(A)⁺RNA. Autoradiograms were exposed for 48 h at -70 °C. The blots were re-probed with a β-actin cDNA probe for control. *sk. muscle*: skeletal muscle, *sm. intestine*: small intestine, *PBL*: peripheral blood leukocytes.

On page 7, please replace the last paragraph with the following:

- Figures 11A-11D show the distribution of TASK mRNA in adult mouse. **A:** Northern blot analysis. Each lane contains 2 μ g of poly(A)⁺RNA. Autoradiograms were exposed for 72 h at -70 °C. The blots were re-probed with a β -actin cDNA probe for control. **B, C, D:** *in situ* hybridization analysis from a coronal section at the level of the forebrain (B), the cerebellum (C), and the heart (D) using the antisense oligonucleotide (SEQ ID NO:24). Warmer colors represent higher levels of expression. *CA1-CA3:* fields CA1-3 of Ammon's horn, *Cx:* cerebral cortex, *DG:* dentate gyrus, *GI:* granular layer, *Hb:* habenula, *SN:* substantia nigra, *PLCo:* postero lateral cortical amygdaloid nuclei, *PVP:* paraventricular thalamic nucleus, *A:* atrium, *V:* ventricle.